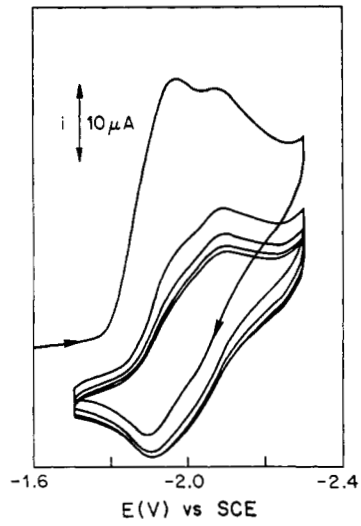

Figure 2. Cyclic voltammogram of 1.0 mM 1 in DMF (0.10 M tetra-*n*-butylammonium tetrafluoroborate) at glassy carbon with ν = 200 mV s^{-1}.

wave A shifts cathodically with increasing ν (−70 mV/decade). In contrast, wave C shifts only 30 mV/decade in the anodic direction with increasing ν. Both A and C would be expected to shift in opposite directions by the same amount if they represented a quasi-reversible couple. More compelling evidence for the postulate that waves A and C are not coupled is shown in Figure 2. A CV of 1 (1.0 mM) in DMF (0.10 M tetra-*n*-butylammonium tetrafluoroborate) at a scan rate of ν = 200 mV s^{-1} shows that repetitive scans between −1.7 and −2.3 V rapidly deplete the concentration of 1 at the electrode surface resulting in a large decrease in current for wave A. In contrast, the currents at waves B and C are less affected and tend to remain constant after several cycles. Thus, it is evident that wave C is not coupled to wave A, but is coupled to wave B.

Conclusion

One possible picture that emerges from the ESR and electrochemical data is summarized in eq 2. Compound

$$1 \xrightarrow[\text{(wave A)}]{2e^-/2H^+} 2 \underset{-e^- \text{ (wave C)}}{\overset{e^- \text{ (wave B)}}{\rightleftharpoons}} 2^{-\cdot} \qquad (2)$$

1 is reduced irreversibly at wave A to its dihydro derivative 2. Although a DISP2 mechanism[17] for this first-order $2e^-/2H^+$ process can be eliminated, the ECEC, EECC, and DISP1 mechanisms cannot be distinguished. Compound 2 is then reduced to its relative stable radical anion ($2^{-\cdot}$), which gives the quasi-reversible couple at waves B and C, in reasonable agreement with the $E_{1/2}$ of −1.91 V (SCE) reported for $2^{-\cdot}$ (Me_2SO) in the literature.[5]

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Registry No. 1, 30735-61-6; $1^{-\cdot}$, 96845-63-5; 2, 41232-69-3; 7, 84-54-8.

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Enantioselective Reduction of Ketones with Reagents from Lithium Aluminum Hydride and Axially Chiral 2,2′-Diamino-1,1′-binaphthyls

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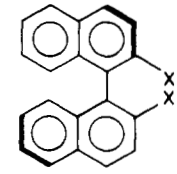
The enantioselective reduction of an achiral carbonyl compounds by a chiral hydride reagent has been the subject of much study. So far, various types of chiral ligands with centro chirality have been developed.[1] Axially chiral 2,2′-dihydroxy-1,1′-binaphthyl (**1f**) has been used for the

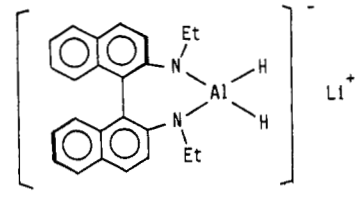


1a, X = NH_2
b, X = NHMe
c, X = NHEt
d, X = NH-*i*-Bu
e, X = $NHCH_2Ph$
f, X = OH

formation of a chiral $LiAlH_4$ complex having an excellent enantioselectivity in the reduction of phenyl alkyl ketones,[2] whereas similar types of diamino analogue, 2,2′-diamino-6,6′-dimethyl-1,1′-biphenyl, afforded a moderate one.[3]

Recently, we have synthesized various 2,2′-bis(alkylamino)-1,1′-binaphthyls **1b–e** with axial chirality in order to examine their usefulness as a chiral aminophosphine ligand of homogeneous Rh catalyst for the asymmetric hydrogenation of prochiral olefins.[4] In this paper, we wish to report an enantioselective reduction of various ketones with reagents from $LiAlH_4$ and (*R*)-**1a–e**. Compounds **1b–e** were prepared from homochiral (*R*)-**1a** by acylation and subsequent $LiAlH_4$ reduction.

A typical example for the preparation of a chiral lithium aluminum hydride reagent is as follows. To a stirred, standardized solution of $LiAlH_4$ in THF[5] was added equimolar amount of homochiral *R* diamine **1c** in THF at 0 °C; then the solution was kept at 60 °C for 40 min. Two molar equivalents of hydrogen evolved to give a homogeneous solution suggesting that the active species in the hydride solution is **2**. The complex thus formed does not separate even at −100 °C.



2

We have now carried out experiments designed to explore the effects of steric bulk of the substituents in the chiral amine ligands, temperature, solvents, additive, and various substrates upon the selectivity of this reduction.

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Table I. Enantioselective Reduction of Ketones with Chiral $LiAlH_4$–2,2′-Diamino-1,1′-binaphthyl 1a–e Complexes[a]

entry	substr	chiral diamine ligand[d]	solvent (additive)	temp, °C	convn, %[b]	config of ROH	enantioselectivity, % ee
1	PhCOEt	(*R*)-**1a**	THF	−78	100	*R*	9
2	PhCOEt	(*R*)-**1a**	THF (EtOH)	−78	96	*R*	3
3	PhCOEt	(*R*)-**1a**	Et_2O	RT[e]	96	*R*	1
4	PhCOEt	(*R*)-**1b**	THF	−78	100	*S*	23
5	PhCOEt	(*R*)-**1b**	THF (EtOH)	−78	98	*S*	13
6	PhCOEt	(*R*)-**1c**	THF	−78	100	*S*	49
7	PhCOEt	(*R*)-**1c**	THF	−100	99	*S*	72[c]
8	PhCOEt	(*R*)-**1c**	Et_2O	−78	100	*S*	45
9	PhCOEt	(*R*)-**1c**	$PhCH_3$	−78	97	*S*	45
10	PhCOEt	(*R*)-**1d**	THF	−78	99	*S*	32
11	PhCOEt	(*R*)-**1e**	THF	−78	100	*S*	14
12	PhCOMe	(*R*)-**1c**	THF	−100	99	*S*	43[c]
13	PhCO-*i*-Pr	(*R*)-**1c**	THF	−100	100	*S*	82[c]
14	PhCO-*t*-Bu	(*R*)-**1c**	THF	−100	98	*S*	56[c]
15	n-$C_6H_{13}COMe$	(*R*)-**1c**	THF	−100	100	*S*	15[c]

[a] Molar ratio of LAH:diamine:ketone = 1:1:0.3. [b] Determined by GLC analysis (PEG 20 M). [c] % ee was also determined by MTPA/LSR method. [d] Satisfactory analytical data (±0.4% for C, H, N) were reported for all optically active diamines listed above except for (*R*)-(+)-**1e**. The racemic **1e** gave a satisfactory result. [e] Room temperature.

The chiral ligands can be recovered from the reduction mixture without loss of their enantiomeric purity by 6 N hydrochloric acid extraction and can be used repeatedly. The results are summarized in Table I.

Several interesting observations can be drawn from Table I. (1) The sense and the magnitude of enantioselectivity are substantially affected by steric bulk of the alkyl group in the chiral amine ligands; reduction with the chiral hydride complex from (*R*)-2,2′-diamino-1,1′-binaphthyl (**1a**) afforded *R* alcohols (entries 1 and 3) revealing the same sense of the induction with that from **1f**.[2] On the other hand, introduction of an alkyl group to the amino function (**1b–e**) reverses the sense of the chiral induction as is observed in entries 4–11. (2) The highest enantioselectivity (82% ee) was attained for isobutyrophenone with the complex prepared from (*R*)-2,2′-bis(ethylamino)-1,1′-binaphthyl (**1c**, X = NHEt) in THF at −100 °C, and when the steric bulk of the alkyl group in the chiral amine ligand becomes smaller or larger than that of Et group, the selectivity goes down (Figure 1). (3) Addition of 1 mol equiv of EtOH to the complexes prepared from **1a** and **1b** lowers the degree of the asymmetric bias (entries 2 and 5), contrary to the observation in the case of the LAH complex from **1f**[2] where the selectivity dramatically increased by the addition of 1 mol equiv of EtOH. (4) The degree of asymmetric induction also depends on the steric bulk of the alkyl group in phenyl alkyl ketone; the selectivity increases with increasing steric bulk of the alkyl group (entries 12, 7, 13, and 14) and becomes maximum when R = *i*-Pr (Figure 1). (5) Among the solvents examined, THF gave the best result as compared to other solvents.

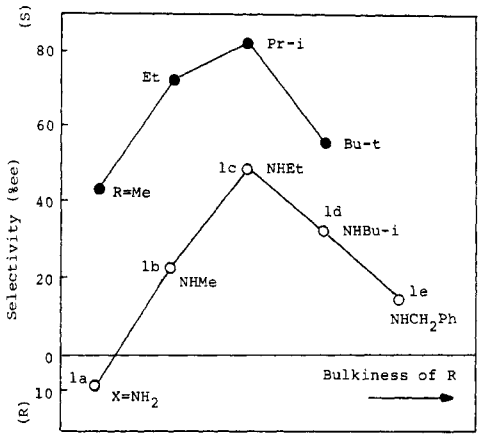

Figure 1. Dependence of enantioselectivity on the steric bulk of the alkyl group in chiral amine ligands and phenyl alkyl ketones: (○) reduction of PhCOEt with $LiAlH_4$–chiral amine, **1a–e** complexes at −78 °C in THF; (●) reduction of PhCOR with $LiAlH_4$–**1c** complex at −100 °C in THF.

Experimental Section

Instruments. NMR spectra were taken on a 90-MHz spectrometer. Optical rotations were taken on a electronic polarimeter using 1-dm thermostated microcell. GLC analyses were made by using PEG 20 M, 3 mm × 1.5 m column.

Solvent and Reagent. Diethyl ether and THF were distilled over $LiAlH_4$. Toluene was distilled over NaH. All of the solvents were stored over Linde molecular sieves 3A. A stock $LiAlH_4$ solution in ether or THF was passed through a glass filter under nitrogen and stored in a flask closed with a rubber septum.[5] It was analyzed by iodometry[6] immediately prior to use. Aliquots were removed by syringe as needed.

Chiral Amine Ligands 1a–e. (*R*)-2,2′-Diamino-1,1′-binaphthyl (**1a**) was prepared by the method previously described,[4] and samples which showed $[\alpha]^{22-24}_D$ (+159±2° (*c* 0.5–0.8, pyridine) were used as homochiral **1a** for the subsequent reaction. The following (*R*)-2,2′-bis(alkylamino)-1,1′-binaphthyls **1b–e** were obtained from **1a** by acylation and subsequent $LiAlH_4$ reduction: **1b**, mp 142.5–143 °C, $[\alpha]^{20}_D$ +178° (*c* 1.07, PhH); **1c**, mp 40–42 °C, $[\alpha]^{20}_D$ +165° (*c* 0.976, PhH); **1d**, oil, $[\alpha]^{20}_D$ +140° (*c* 0.803, PhH); **1e**, mp 54–57 °C, $[\alpha]^{20}_D$ +122° (*c* 0.922, PhH). Satisfactory spectral (IR and ^1H NMR) and analytical data were obtained for all of these amines.

The optical purities of the diamine **1b** and **1c** were examined by HPLC under the following conditions: Column, Chiral Pak OT(+) 4.6 × 250 mm; eluent, MeOH; temperature, 5 °C; flow rate, 0.5 mL/min, α 1.68 and 2.19 for (±)-**1b** and (±)-**1c**, respectively.

No detectable peak of the other enantiomer was observed for each optically active diamine, indicating that there was no racemization during the synthesis of the diamines started from optically pure **1a**. From the results, it is assumed that **1d** and **1e** are also enantiomerically pure.

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Asymmetric Reduction of Isobutyrophenone with $LiAlH_4$–Chiral Amine 1c Complex (Representative Example). To a standardized solution of $LiAlH_4$ (1.0 mmol) in THF (2 mL) was added 340 mg (1 mmol) of (*R*)-2,2′-bis(ethylamino)-1,1′-binaphthyl (**1c**) in THF (1.5 mL) at 0 °C; then the solution was kept at 60 °C for 40 min. Two millimoles of hydrogen evolved to give a homogeneous solution. The resulting solution was cooled to −100 °C, a THF solution (0.5 mL) of 44 mg (0.3 mmol) of isobutyrophenone was dropwise added, and the reduction was monitored by GLC. After the reaction mixture was stirred for 4 h, the excess hydride was decomposed by the dropwise addition of water at the temperature. THF was removed under reduced pressure, then the residue was dissolved in 6 N HCl and extracted with ether. The extract was washed with 6 N HCl, saturated $NaHCO_3$, and water, successively, and dried over Na_2SO_4. Ether was removed and the residual oil was distilled in vacuo (~100 °C (5 mmHg)) to give pure (*S*)-2-methyl-1-phenyl-1-propanol: 32 mg (82%), $[\alpha]^{20}_D$ +39.1° (*c* 2.98, ether), 82% ee, determined by both optical rotation[7] and MTPA/LSR method[8] using Mosher's MTPA ester and a NMR shift reagent, $Eu(fod)_3$. From the 6 N HCl fraction, **1c** was recovered in a usual manner: 296 mg (87%), $[\alpha]^{20}_D$ +163° (*c* 1.19, PhH).

Acknowledgment. We thank Dr. A. Ichida, Daicel Chemical Industries, Ltd., for HPLC analysis of the enantiomeric purities of the diamines.

Registry No. (*R*)-**1a**, 18741-85-0; (*R*)-**1b**, 93713-30-5; (*R*)-**1c**, 96998-27-5; (*R*)-**1d**, 96964-14-6; (*R*)-**1e**, 96948-51-5; PhC(O)Et, 93-55-0; PhC(O)Me, 98-86-2; PhC(O)-*i*-Pr, 611-70-1; PhC(O)-*t*-Bu, 938-16-9; *n*-$C_6H_{13}C(O)Me$, 111-13-7; $LiAlH_4$, 16853-85-3; (*R*)-$PhCH(OH)CH_2CH_3$, 1565-74-8; (*S*)-$PhCH(OH)CH_2CH_3$, 613-87-6; (*S*)-$PhCH(OH)CH_3$, 1445-91-6; (*S*)-$PhCH(OH)CH(CH_3)_2$, 34857-28-8; (*S*)-$PhCH(OH)C(CH_3)_3$, 24867-90-1; (*S*)-$CH_3(CH_2)_5CH(OH)CH_3$, 6169-06-8.

(7) Maximum rotation of PhCH(OH)Me, $[\alpha]^{20}_D$ 42.2° (*c* 2.0, MeOH), this work. PhCH(OH)Et, PhCH(OH)-*i*-Pr, PhCH(OH)-*t*-Bu: MacLeod, R.; Welch, F. J.; Mosher, H. S. *J. Am. Chem. Soc.* **1960**, *82*, 876. $C_6H_{13}CH(OH)CH_3$: Hill, R. K. *J. Am. Chem. Soc.* **1958**, *80*, 1611.

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Light-Catalyzed and Silver Acetate Catalyzed Oxidation of Alcohols with *N*-Iodosuccinimide: Two Different Pathways

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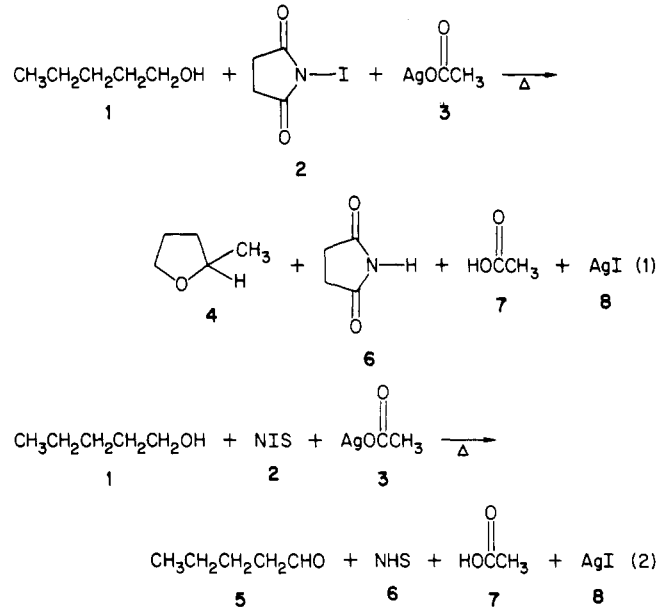
In past years, we have studied the reaction of primary,[1] secondary,[2] and tertiary[3] alcohols with *N*-iodosuccinimide (NIS) and irradiation. The identity of the products obtained suports the belief[4] that alkyl hypoiodities are formed when alcohols and NIS react. Irradiation of the intermediate hypoiodities homolytically cleaved the oxygen–iodine bond which gave final products from the decomposition of the alkoxy radical intermediates.

In this study we have oxidized a variety of alcohols with NIS in the presence of silver acetate but in the absence of light. The obtained products, substantially different from those found when the same alcohols were oxidized with NIS and irradiation (Table I), indicate a silver ion catalyzed[5] decomposition pathway for the alkyl hypoiodite. Three primary alcohols (1-pentanol, 1-butanol, and 3-methyl-1-butanol), which were treated with the NIS–silver acetate method, gave a mixture of tetrahydrofuran and aldehyde products. Irradiation of these same alcohols with NIS gives only the tetrahydrofuran products.

The formation of primary alcohol oxidation products can be illustrated by a discussion of the oxidation of 1-pentanol (**1**) with NIS (**2**) and silver acetate (**3**). When the alcohol **1** is dissolved in benzene and mixed with **2** and **3** and heated, both 2-methyltetrahydrofuran (**4**) (22–37%) and pentanal (**5**) (25–40%) are formed as shown in eq 1 and 2, respectively. The stoichiometry shown in eq 1 and 2 is supported by good yields of succinimide (**6**), acetic acid (**7**), and silver iodide (**8**).



The reaction of alcohols with bromine and silver salts[5] and iodine and mercuric oxide[6] to produce tetrahydrofuran products has been reported by many authors. Several of these investigators[5b,f] have suggested ionic pathways for the production of the tetrahydrofurans when silver and mercury salts have been present. Our *N*-iodosuccinimide oxidation of alcohols in the presence of silver acetate may also be heterolytic in nature.

When the secondary alcohols were heated with NIS and silver acetate, the product composition again indicated hypoiodiate formation followed by silver acetate decomposition of the hypoiodite. Cyclopentanol produced cyclopentanone in 30–45% yields. No cyclopentanone is found when NIS and light are used. When cyclopentanol is treated with NIS and light, ring opening predominates

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